UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Ex parte ISIDORE RIGOUTSOS,
YUAN GAO, and ARISTIDIS FLORATOS

Appeal No. 2006-0968
Application No. 09/712,638

ON BRIEF

Before MILLS, GRIMES, and GREEN, Administrative Patent Judges.

GRIMES, Administrative Patent Judge.

DECISION ON APPEAL

This appeal involves claims to a method of comparing sequences of symbols, such as DNA sequences. The examiner has rejected the claims as indefinite, directed to nonstatutory subject matter, anticipated, and obvious. We have jurisdiction under 35 U.S.C. § 134. We reverse the rejection for nonstatutory subject matter, affirm-in-part the rejections for anticipation and indefiniteness, and affirm the rejection for obviousness.

Background

"Sequences of symbols are useful in a number of areas. One such area is DNA. . . . Another area where sequences of symbols are important is proteins."

Specification, page 1. The specification discloses "a way of determining in an unsupervised manner additional members for a family that is defined initially through exemplar sequences." Page 6. "By 'unsupervised' it is meant that no predetermined or a priori information is needed/known about the exemplar sequences or is employed by the discovery process. Additionally, there is no need for user supervision or intervention. For instance, the present invention does not require knowledge of biological information related to the family, aligned sequences, knowledge of properties of the exemplary sequences defining the family, and/or knowledge of the cardinality or characteristics of the exemplar sequences. It is possible to exclude one of more of these restrictions. For instance, the present invention could be used on a set of aligned sequences." Pages 6-7.

Discussion

1. Claim construction

Claims 1-12, 23, and 25 are pending and on appeal. Claims 1-3, 10, 12, 23, and 25 stand or fall together because Appellants have not argued them separately. See 37 CFR § 41.37(c)(1)(vii). We will limit our discussion within this group of claims to independent claim 1; claims 2, 3, 10, 12, 23, and 25 will stand or fall with claim 1.

Claims 1, 4-9, and 11 read as follows:

> 1. A method comprising the steps of:
> providing a set of sequences, wherein the sequences are not aligned;
> discovering a plurality of patterns common to a plurality of the sequences; and determining if a candidate sequence comprises a predetermined number of the patterns.
>
> 4. The method of claim 1, wherein the step of discovering is performed without using any knowledge about properties or features of sequences in the set of unaligned sequences.

5. The method of claim 1, further comprising the steps of:
if the candidate sequence comprises the predetermined number of patterns, adding the candidate sequence to the set of sequences to create a new set of sequences; and
performing the step of discovering on the new set of sequences.

6. The method of claim 1, wherein each sequence comprises a series of symbols and wherein each pattern comprises a plurality of positions, some of the plurality of positions each comprise at least one expected symbol and other of the plurality of positions comprise positions which may be occupied by any sequence character.

7. The method of claim 6, wherein, for one of the positions, the at least one expected symbol is a plurality of expected symbols.

8. The method of claim 3 [the method of claim 1, further comprising the step of determining if each of the plurality of patterns is statistically significant], wherein the step of determining if each of the plurality of patterns is statistically significant comprises the steps of selecting one of the patterns, determining if a probability that the selected pattern occurs in a sequence meets a predetermined threshold, and continuing to select additional patterns until each pattern has been selected.

9. The method of claim 8, wherein the step of determining if a probability that the selected pattern occurs in a sequence meets a predetermined threshold further comprises the steps of using a second-order Markov chain method to determine the probability that the selected pattern occurs in a sequence and determining a natural logarithm of the probability that the selected pattern occurs in a sequence.

11. The method of claim 3, wherein the step of determining if each of the plurality of patterns is statistically significant further comprises the steps of if any of the patterns is statistically significant, selecting a statistically significant pattern, modifying a composite descriptor to include the selected pattern if the selected pattern is not already part of the composite descriptor, and continuing to select statistically significant patterns until all statistically significant patterns have been selected.

Claim 1 includes the transition term "comprising," meaning that the claimed process includes all of the recited steps and can also include additional steps. For example, the method can include a step of aligning the sequences in the unaligned set

of sequences provided in the first step. See the specification, page 7, lines 1-2 ("[T]he present invention could be used on a set of aligned sequences."). Claim 1 does not recite any particular method(s) of discovering common patterns or determining if a candidate sequence shares any of the patterns. In addition, claim 1 does not require that the candidate sequence share any "predetermined number of patterns" with the set of sequences, so a method that determines that a candidate sequence does not share any of the patterns common to a set of sequences would meet the limitations of the third step of the claimed method.

Thus, claim 1 is broadly directed to a method comprising providing a set of unaligned sequences of symbols, discovering patterns common to at least some of the symbols, and determining whether or not a candidate sequence includes any of the patterns.

Claim 4 adds the limitation that the discovering step "is performed without using any knowledge about properties or features of sequences in the set of unaligned sequences."

Claim 5 adds to claim 1 the following steps: if the candidate sequence is found to share "the predetermined number of patterns," it is added to the original set of sequences and the discovering step is performed on the new set of sequences.

Claim 6 depends on claim 1 and adds the limitations that "each sequence comprises a series of symbols," and each pattern comprises some positions that "each comprise at least one expected symbol" and others can comprise any symbol (so-called "don't-care" positions; specification, page 2, lines 4-6).

Claim 7 depends on claim 6 and adds the requirement that "for one of the positions, the at least one expected symbol is a plurality of expected symbols."

Claims 8 and 11 add to claim 1 the step of determining if each of the patterns shared by the set of sequences is statistically significant by a recited method (claim 8) and using statistically significant patterns to modify a composite descriptor (claim 11). A composite descriptor is a set of patterns shared by a set of sequences. Specification, page 1-2 ("One method is to determine a pattern of symbols that all of the sequences share. This is called the single descriptor approach. . . . The composite descriptor method examines a candidate protein for several alphabetic patterns, as opposed to only one pattern with the single descriptor method.").

Claim 9 depends on claim 8 and adds the steps of "using a second-order Markov chain method . . . and determining a natural logarithm of the probability that the selected pattern occurs in a sequence."

2. Definiteness

The examiner rejected claims 4 and 7 under 35 U.S.C. § 112, second paragraph, as indefinite. The examiner argued that claim 4 is indefinite for two reasons: first, because it refers to "unaligned sequences" while claim 1 refers to sequences that are "not aligned," and it is unclear whether the two phrases are synonymous; and, second, because it states that the method is carried out "without using any knowledge about properties or features of sequences in the set of unaligned sequences," but the knowledge that the sequences are unaligned, as required by claim 1, is knowledge about the properties or features of the sequences. Examiner's Answer, pages 3-4.

We do not agree with the examiner that the phrase "unaligned sequences" in claim 4 makes the claim indefinite. A person of ordinary skill in the art would recognize that the "unaligned sequences" in claim 4 are the same as the "sequences [that] are not aligned" in claim 1. We therefore reverse that basis of the rejection.

However, we agree with the examiner that claim 4 is indefinite because of its requirement that "the step of discovering is performed without using any knowledge of the properties or features of sequences in the set of unaligned sequences." The specification provides no definition of "properties" or "features" that would limit the type of information referred to in claim 4. The specification states that

> it is not easy to define what a feature is. The definition of a feature is directly related to the representation of the items that are studied, i.e., the way each of the objects processed by the system . . . is represented and stored in a computer. . . . For instance, for a helix-turn-helix (HTH) motif that mediates the binding of many regulatory proteins to regulatory control sites of DNA, the two features are the two helices at the beginning (7 a.a.) and the end (9 a.a.) of the 20 a.a. stretch that corresponds to an instance of the HTH motif. . . . [F]or some applications, individual a.a. letters can be thought of as "features."

Pages 7-8. Similarly, the specification offers no limiting definition of "properties," stating only that

> [a] property can be thought of as an attribute of a feature: in the case of the HTH, a property would be the fact that the two features (helices) are held together through non-polar interactions of their side chains.

Page 7, lines 23-25.

During examination, claims are given their broadest reasonable interpretation consistent with the specification. See, e.g., In re Morris, 127 F.3d 1048, 1054, 44 USPQ2d 1023, 1027 (Fed. Cir. 1997). We therefore interpret claim 4's recitation of "properties or features" of sequences to include the sequence of letters (e.g., DNA

bases or amino acids) that make up the unaligned sequences: the order of the bases or amino acids in the sequences reasonably appears to be a property or feature of the unaligned sequences.

When claim 4 is given its broadest reasonable interpretation, however, it is inconsistent with claim 1, which requires "providing a set of sequences" and "discovering a plurality of patterns common to a plurality of the sequences." These steps reasonably appear to require knowing which sequences are being provided and compared. If the sequences are known, however, the discovering step cannot be performed as required by claim 4 – "without using any knowledge of the properties or features of [the] sequences."

Since the broadest reasonable interpretation of claim 4 is inconsistent with the claim on which it depends, we agree with the examiner that claim 4 is indefinite. The basis for our conclusion, however, differs from that of the examiner (who focused on the fact that the sequences were known to be unaligned). For this reason, the arguments that Appellants have made in response to the rejection are not germane to the rationale on which we rely.

Since Appellants have not had a fair opportunity to respond to the rejection, we designate our affirmance (with respect to this rejection) as a new ground of rejection. See In re Kronig, 539 F.2d 1300, 1302-03, 190 USPQ 425, 426-27 (CCPA 1976).

The examiner also rejected claim 7 as indefinite. Claim 7 states that "for one of the positions, the at least one expected symbol is a plurality of expected symbols." The examiner stated that the claim is "vague and indefinite because it is unclear whether

'one of the positions' is occupied by one symbol or a plurality of symbols." Examiner's Answer, page 4.

Appellants argue that "this limitation of claim 7 refers to the pattern(s). The specification, at page 13, lines 1-3, for example, indicates that a bracket, e.g., in a pattern, represents a 'one of' choice. For instance, the exemplary pattern shown in the specification, at page 25, line 21, illustrates some positions being occupied by 'one of' a plurality of symbols. As such the limitations of claim 7 are not indefinite." Appeal Brief, page 5.

We agree with Appellants that, when claim 7 is read in light of the specification, its meaning is reasonably clear. The specification states that a "." in a pattern "is used to denote a position in a sequence or pattern that can be occupied by an arbitrary residue. A bracket is meant to denote a 'one of' choice; i.e., [KR] means that the position this bracket corresponds to can be occupied by exactly one of K or R." Pages 12-13.

The exemplary pattern on page 25, line 22, illustrates these principles. The pattern includes the following subsequence: F....[ILMV]. For the first position in this subsequence, the expected symbol is "F", which is followed by four "don't care" positions, and, in the last position of the subsequence, the expected symbol is one of I, L, M, or V. The last position is therefore one for which the expected symbol is "a plurality of expected symbols," as recited in claim 7.

"The test for definiteness is whether one skilled in the art would understand the bounds of the claim when read in light of the specification." Miles Laboratories Inc. v. Shandon Inc., 997 F.2d 870, 875, 27 USPQ2d 1123, 1126 (Fed. Cir. 1993). That

standard is met here. We reverse the rejection of claim 7 under 35 U.S.C. § 112, second paragraph.

3. Nonstatutory subject matter

The examiner rejected claims 1-12, 23, and 25 under 35 U.S.C. § 101 as being directed to nonstatutory subject matter. The examiner argued that the claims are directed to a method for "analyzing sequence data without any physical alteration step, which is considered to be non-statutory subject matter." Examiner's Answer, page 6. The examiner cited an example from the Manual of Patent Examining Procedure (MPEP) stating that "a computer process that simply calculates a mathematical algorithm that models noise is nonstatutory," and concluded that, like that example, "the instant invention comprises algorithmic steps for analyzing sequence data without any physical alteration result[ing] from said analysis." Id.

Appellants argue that the claims are directed to patentable subject matter because they are directed to a practical application of an abstract idea or mathematical algorithm. Appeal Brief, page 6.

We agree with Appellants that the examiner has not provided an adequate basis on which to conclude that the instant claims are directed to nonstatutory subject matter. The examiner seems to apply a bright-line rule that a computer-based method must result in a physical transformation outside the computer in order to be considered to produce a useful, concrete, and tangible result and thereby satisfy 35 U.S.C. § 101.

The examiner cites MPEP § 2106(IV)(B)(2)(b) as the source of this perceived rule. That section of the MPEP does not support the examiner's position. It states that "[t]o be statutory, a claimed computer-related process must either: (A) result in a

physical transformation outside the computer . . . or (B) be limited to a practical application within the technological arts" (emphasis added).[1]

With regard to the latter, the MPEP states that a "process that merely manipulates an abstract idea or performs a purely mathematical algorithm" is nonetheless statutory if "the claimed process [is] limited to a practical application of the abstract idea or mathematical algorithm in the technological arts. . . . A claim is limited to a practical application when the method, as claimed, produces a concrete, tangible and useful result; i.e., the method recites a step or act of producing something that is concrete, tangible and useful." MPEP § 2106(IV)(B)(2)(b)(ii).

In addition, we note that the section of the MPEP cited by the examiner has been superseded by the Interim Guidelines for Examination of Patent Applications for Patent Subject Matter Eligibility, 1300 Off. Gaz. Pat. Office 142 (November 22, 2005) (accessible on-line at www.uspto.gov/go/og/2005/week47/patgupa.htm). The Interim Guidelines expressly state that "physical transformation 'is not an invariable requirement, but merely one example of how a mathematical algorithm [or law of nature] may bring about a useful application.'" Id. at 146[2] (quoting AT&T Corp. v. Excel Commc'ns, Inc., 172 F.3d 1352, 50 USPQ2d 1447 (Fed. Cir. 1999), alteration in original). The Interim Guidelines state that a process that does not result in physical transformation may nonetheless be statutory if it achieves a useful, concrete and tangible result. Id.

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[1] The examiner at one point acknowledged these alternatives, but stated that "[t]he claimed method does not satisfy either one of the recited requirements," without any explanation of why the claims are not directed to a practical application. Examiner's Answer, page 8. Such a conclusory statement does not satisfy the examiner's burden of showing prima facie unpatentability.

[2] Page 20 of the on-line version of the Interim Guidelines.

The Interim Guidelines also define the terms "useful", "concrete", and "tangible" as they are to be applied during examination. See id. We note that the terms "tangible" and "concrete" do not require physical transformation of objects outside the computer. See id.[3] ("The tangible requirement does not necessarily mean that a claim . . . must operate to change articles or materials to a different state or thing" and to "produce[ ] a 'concrete' result . . . the process must have a result that can be substantially repeatable or the process must substantially produce the same result again.").

The Interim Guidelines, in analyzing the relevant case law, provide the following guidance for determining whether a claimed process is statutory: "The focus of the inquiry is on whether the claim, considered as a whole, constitutes 'a practical application of an abstract idea.' . . . [A]n 'abstract idea' when practically applied to a useful end is eligible for a patent." Id. at 149.[4] "The focus is not on whether the steps taken to achieve a particular result are useful, tangible and concrete, but rather that the final result is 'useful, tangible and concrete.'" Id.[5]

Here, the claimed process discovers patterns common to a set of sequences, and determines whether a candidate sequence includes the common pattern(s). The specification states that the claimed method is useful for, among other things, grouping sequences such as DNA or protein sequences, into families that are expected to share similar properties. See page 1, lines 9-14 and 21-27.

The examiner has not adequately explained why the claimed process does not produce a result that is useful, tangible, and concrete, as those terms are defined in the

[3] Page 21 of the on-line version of the Interim Guidelines.
[4] Page 37 of the on-line version of the Interim Guidelines.
[5] Page 38 of the on-line version of the Interim Guidelines.

Interim Guidelines. Because the examiner has the initial burden of showing unpatentability, see In re Brana, 51 F.3d 1560, 1566, 34 USPQ2d 1436, 1441 (Fed. Cir. 1995), and that burden has not been carried here, we reverse the rejection of claims 1-12, 23, and 25 under 35 U.S.C. § 101.

4. Anticipation

The examiner rejected claims 1-8, 10-12, 23, and 25 under 35 U.S.C. § 102(b) as anticipated by Benson.[6] The examiner noted that Benson discloses that "GenBank compris[es] over 600 million nucleotide bases, and a subset of GenBank is the UniGene collection of unique human gene sequences." Examiner's Answer, page 9. The examiner relied on NCBI News[7] as evidence of "the inherent characteristics of the UniGene Collection as cited by Benson." Id. The examiner cited NCBI News' teaching that "[t]he UniGene set serves . . . as a standard to compare and screen new EST submissions. New EST submissions that do not match any sequences in the UniGene set are considered new genes and are organized into unique clusters." Examiner's Answer, pages 9-10.

Finally, the examiner cited Benson's disclosure that GenBank is used for sequence similarity searching using, e.g., "the BLAST family of search programs." Examiner's Answer, page 10. The examiner cited Altschul[8] as evidence that searching using BLAST meets the limitations of the instant claims: "In BLAST, statistical significance scores are calculated [as] a set of probabilities for the occurrence of

[6] Benson et al., "GenBank," Nucleic Acids Research, Vol. 25, pp. 1-6 (1997)
[7] NCBI News, pages 1-18, August 1996
[8] Altschul et al., "Basic local alignment search tool," J. Mol. Biol., Vol. 215, pp. 403-410 (1990)

individual residues (at least one expected symbol), and for aligning pairs of residues (plurality of positions)." Id.

We agree with the examiner that Benson, as evidenced by the other cited references, reasonably appears to anticipate claim 1. As discussed above, claim 1 is directed to a process comprising providing a set of unaligned sequences of symbols, optionally aligning the sequences, discovering pattern(s) common to at least some of the sequences, and determining whether a candidate sequence includes the pattern(s).

Benson describes the process by which the UniGene collection was created: "UniGene starts with human entries in the primate (PRI) division of GenBank [and] combines these with human ESTs." Benson, page 2, right-hand column. This description reasonably appears to correspond to providing a set of unaligned sequences of symbols.

Next, UniGene "creat[es] clusters of sequences that share virtually identical 3' untranslated regions (3' UTRs)." Id. This description reasonably appears to be a step of discovering patterns common to at least some of the sequences, as required by claim 1. The sequences may or may not be aligned during the process of matching 3' UTRs but claim 1 is open to either approach.

Finally, NCBI News describes how the UniGene collection was used by those skilled in the art: "The UniGene set serves . . . as a standard to compare and screen new EST submissions. New EST submissions that do not match any sequences in the UniGene set are considered new human genes and are organized into unique clusters." Pages 3-4. This description reasonably appears to be a step of determining if a candidate sequence (new EST) comprises a predetermined number of patterns (i.e., if it

comprises any of the known 3' UTRs). Thus, Benson's disclosure of the UniGene collection, in view of the evidence that the collection was used to categorize new ESTs, reasonably appears to meet all the limitations of instant claim 1.

Appellants argue that "nowhere does Benson teach or suggest discovering any patterns. Clustering similar sequences simply is not the same as pattern discovery, even if the clustering is based on 'significant DNA similarity.' For at least that reason, the teachings of [claims 1-3] are neither anticipated nor obvious over Benson." Appeal Brief, page 7.

We do not find this argument persuasive. Benson describes clustering sequences together based on their "virtually identical 3' untranslated regions." A set of sequences sharing virtually identical 3' UTRs would reasonably appear to share at least one common "pattern." Appellants have pointed to no definition of "patterns" in the specification that would exclude a set of "virtually identical 3' untranslated regions." During examination, claims are given their broadest reasonable interpretation consistent with the specification. In re Morris, 127 F.3d 1048, 1054, 44 USPQ2d 1023, 1027 (Fed. Cir. 1997). Appellants have pointed to no disclosure in the specification that is inconsistent with construing "patterns" to include "virtually identical 3' untranslated regions." Therefore, we conclude that claim 1 reads on the prior art disclosure.

With regard to claim 5,[9] Appellants argue that

> Benson does not teach or suggest setting a "predetermined number" criteria. By way of example only, NCBI News, in a more detailed explanation of the teachings of Benson, merely states that sequences

[9] Appellants also argue claim 4 separately. However, since we have concluded that claim 4 is indefinite, we do not reach the issue of whether it is anticipated. See In re Steele, 305 F.2d 859, 862, 134 USPQ 292, 295 (CCPA 1962) (rejecting indefinite claims over prior art, based on speculation and assumptions, is legal error).

> sharing statistically significant DNA sequence similarity in the 3' UTR are assigned to the same cluster. . . . Therefore, no predetermined number criteria, as in the present claims, is employed.

Appeal Brief, page 7.

We do not find this argument persuasive. Claim 5 is directed to the method of claim 1, with the addition step of, "if a candidate sequence comprises the predetermined number of patterns, adding the candidate sequence to the set of sequences to create a new set of sequences; and performing the step of discovering on the new set of sequences." A "predetermined number of patterns" includes one pattern. Thus, when (as described by NCBI News) new ESTs are compared to the UniGene collection to see if their 3' UTRs match the 3' UTR in any of the known clusters, the new ESTs are being determined to compared to a "predetermined number of patterns"; specifically, each of the 3' UTRs in the UniGene collection.

NCBI News states that

> [t]he UniGene set serves . . . as a standard to compare and screen new EST submissions. New EST submissions that do not match any sequences in the UniGene set are considered new human genes and are organized into unique clusters to provide additional mapping candidates. To date, more than 48,000 3'-anchored UniGene clusters have been generated. Some clusters contain more than 1,000 ESTs.

That is, NCBI News describes a process including the steps of determining whether a new EST (candidate sequence) comprise the pattern of any of the known clusters in the UniGene collection. If it does, it is added to that cluster to generate a new set of sequences (the previous UniGene collection plus the new EST). If it does not match any existing cluster, it is organized into a new cluster. In our view, this disclosure describes the additional steps recited in claim 5.

With regard to claim 6, Appellants argue that "BLAST does not involve pattern discovery. . . . BLAST does not generate anything, pattern or otherwise, from the sequences in a set of sequences. BLAST is in fact a query-driven method that involves processing a query sequence to aid in finding matches with that query in a database of sequences. . . . Therefore, BLAST does not anticipate discovering patterns common to a plurality of sequences in a set of sequences and then determining if a candidate sequence comprises a number of the patterns." Appeal Brief, page 9. Appellants rely on the same basic argument with respect to claim 7. Id., pages 9-10.

We agree with Appellants that the examiner has not adequately explained how Benson discloses a process meeting all the limitations of claims 6 and 7, even with the further elaboration provided by Altschul. As noted by the examiner, Benson discloses the use of GenBank for sequence similarity searching using BLAST. Altschul describes how BLAST performs sequence comparison. The process described by Altschul, however, does not appear to involve the method defined by claim 6: discovering patterns common to a set of sequences and determining whether a candidate sequence includes the pattern(s), where the pattern includes both "don't care" positions and positions having an expected symbol.

Rather, the process described by Altschul appears to involve comparing a candidate sequence to a sequence in a database. See page 404, left-hand column: "Many similarity measures, including the one we employ, begin with a matrix of similarity scores for all possible pairs of residues. . . . [T]he similarity score for two aligned segments of the same length is the sum of the similarity values for each pair of aligned residues."

For example, Altschul reports the "[p]erformance of BLAST with homologous sequences." Page 408. Altschul describes searching a set of related sequences (e.g., globins) with a sequence known to be homologous (e.g., woolly monkey myoglobin) and reports how many of the sequences in the data set showed similarity scores above a certain cut-off. The reported results show that the candidate sequence was compared individually to each of the sequences in the data set.

By contrast, the method defined by claim 6 requires discovering a pattern common to the sequences in the data set, where the pattern includes both "don't care" positions and positions having an expected symbol, then determining if a candidate sequence includes the pattern that is common to at least some of the sequences in the data set. Claim 7 includes the same limitations by virtue of its dependence on claim 6. The examiner has not adequately explained how these limitations are taught by Benson, alone or with the evidence provided by Altschul. We therefore reverse the rejection of claims 6 and 7.

With regard to claims 8 and 11, Appellants argue that Benson does not teach the additional steps recited in these claims. See the Appeal Brief, page 8.

Claim 8 is directed to the method of claim 1, further comprising determining if each of the plurality of patterns is statistically significant by "selecting one of the patterns, determining if a probability that the selected pattern occurs in a sequence meets a predetermined threshold, and continuing to select additional patterns until each pattern has been selected."

We agree with the examiner that Benson, as evidenced by NCBI News, reasonably appears to disclose a process comprising the recited steps. NCBI News

states that "[t]he UniGene set serves . . . as a standard to compare and screen new EST submissions. New EST submissions that do not match any sequences in the UniGene set are considered new human genes and are organized into unique clusters." Pages 3-4. This disclosure reasonably appears to describe a step of determining whether each of the known 3'UTRs occurs in a candidate sequence (new EST).

That is, as described by NCBI News, those skilled in the art used the Unigene collection to categorize new ESTs by comparing the sequence of the new EST to each of the known 3' UTRs that are indicative of clusters of ESTs corresponding to separate genes. This process reasonably appears to include the steps of

- "selecting one of the patterns" (i.e., one of the known 3' UTRs);
- "determining if a probability that the selected pattern occurs in a sequence meets a predetermined threshold" (i.e., determining whether a virtually identical sequence occurs in a new EST); and
- "continuing to select additional patterns until each pattern has been selected" (i.e., comparing the other known 3' UTRs to the candidate EST).

Therefore, Benson's disclosure of the UniGene collection, in view of the evidence that the collection was used to categorize new ESTs, reasonably appears to meet all the limitations of instant claim 8.

Claim 11 is another matter. Claim 11 requires, among other things, "modifying a composite descriptor to include the selected pattern if the selected pattern is not already part of the composite descriptor," based on shared, statistically significant patterns. The examiner has pointed to nothing in Benson, alone or as further explained by NCBI News or Altschul, that teaches modifying a composite descriptor based on patterns shared by a set of sequences (UniGene) and a candidate sequence (EST). We therefore reverse the rejection of claim 11.

To summarize, we affirm the rejection under 35 U.S.C. § 102(b) of claims 1, 5, and 8. Claims 2, 3, 10, 12, 23, and 25 fall with claim 1 because they were not argued separately. See 37 CFR § 41.37(c)(1)(vii). We reverse the rejection as applied to claims 6, 7, and 11. We do not reach the merits of the rejection as applied to claim 4 because that claim is indefinite.

5. Obviousness

The examiner rejected claims 1-12 under 35 U.S.C. § 103 as obvious in view of Benson and Kleffe.[10] We have already determined that claims 1-3, 5, 8, 10, and 12 are anticipated by Benson. We therefore affirm the rejection of claims 1-3, 5, 8, 10, and 12 as obvious in view of Benson and Kleffe: "anticipation is the epitome of obviousness." Connell v. Sears, Roebuck & Co., 722 F.2d 1542, 1548, 220 USPQ 193, 198 (Fed. Cir. 1983).

However, we reversed the rejection of claims 6, 7, and 11 as anticipated by Benson. The examiner has pointed to nothing in Kleffe that would remedy the deficiencies of Benson with respect to these claims and Appellants argue that "Kleffe does not provide any of the limitations for which Benson is lacking." Appeal Brief, page 10. We agree with Appellants that the examiner has not made out a prima facie case of obviousness with respect to claims 6, 7, and 11. We therefore reverse the rejection under 35 U.S.C. § 103 with respect to claims 6, 7, and 11.

The only claim that the examiner rejected as obvious but not anticipated is claim 9. Claim 9 is directed to the method of claim 8, and further requires "using a second-

[10] Kleffe et al., "GeneGenerator—a flexible algorithm for gene prediction and its application to maize sequences," Bioinformatics, Vol. 14, pp. 232-243 (1998)

order Markov chain method . . . and determining a natural logarithm of the probability that the selected pattern occurs in a sequence." The examiner reasoned that

> Kleffe et al. discloses an improvement for using second-order Markov chain method to predict gene structure (Abstract etc.). . . . The method of Kleffe et al. requires the use of GenBank sequence information (page 233 . . .). The second-order Markov chain method is used to determine the natural logarithm of the probability of a specific sequence (pattern) occur in the Arabidopsis sequences (pages 242-243 . . .), as in instant claim 9.
>
> An artisan of ordinary skill in the art at the time of the instant invention would have been motivated by the improvement disclosed by Kleffe et al. and utilize the second-order Markov chain method in the method of Benson et al. for discovering new genes.

Examiner's Answer, pages 14-15.

Appellants argue that "[a] review of the teachings of Kleffe . . . reveal[s] no teaching or suggestion of the concept of patterns, but merely the derivation of Markov models using probability functions. As such, Appellants respectfully submit that there is no teaching in Kleffe directed to patterns." Appeal Brief, page 10.

We agree with Appellants that the examiner has not adequately explained how the cited references would have suggested the method of claim 9 to those of ordinary skill in the art. "[I]dentification in the prior art of each individual part claimed is insufficient to defeat patentability of the whole claimed invention. Rather, to establish obviousness based on a combination of the elements disclosed in the prior art, there must be some motivation, suggestion or teaching of the desirability of making the specific combination that was made by the applicant." In re Kotzab, 217 F.3d 1365, 1369-70, 55 USPQ2d 1313, 1316 (Fed. Cir. 2000). "[T]o find a combination obvious there must be some teaching, suggestion, or motivation in the prior art to select the teachings of separate references and combine them to produce the claimed

combination." In re Johnston, 435 F.3d 1381, 1384, 77 USPQ2d 1788, 1790 (Fed. Cir. 2006).

Here, the examiner pointed to Benson for its disclosure (as evidenced by NCBI News) of a method of comparing new ESTs to the UniGene collection as a process the meets all the limitations of claim 1, pointed to Kleffe as disclosing a process that involves a second-order Markov chain method, and concluded that it would have been obvious to combine the two. The problem, however, is that the methods disclosed by Benson (as evidenced by NCBI News) and by Kleffe are directed at analyzing different types of data for different purposes.

As discussed in detail above, the method disclosed by Benson/NCBI News starts with the UniGene collection of clustered ESTs and compares new ESTs with the UniGene data set in order to determine whether the new EST belongs to a previously characterized gene. The process taught by Kleffe, on the other hand, starts with a sequence of genomic DNA and predicts gene structures that could correspond to the genomic sequence. See page 232, right-hand column: "We developed GeneGenerator because of the need for a tool to predict gene structure in maize. . . . Given a certain genome segment thought to contain a gene, our algorithm produces a set of alternative gene predictions that differ in the assignment of splice junctions."

Thus, the processes disclosed by Benson and Kleffe differ in both the starting data and the purpose of analyzing those data. In view of the differences between the disclosed methods, we agree with Appellants that the examiner has not adequately explained why a person of ordinary skill in the art would have been motivated to

combine the method disclosed by Kleffe with the method disclosed by Benson. We therefore reverse the rejection of claim 9 under 35 U.S.C. § 103.

Other Issues

The evidence of record includes Rigoutsos,[11] which appears to be prior art with respect to the instant claims. Rigoutsos describes, among other things, an experiment in which twenty sequences from the core histone H3 and H4 families were analyzed for shared patterns of amino acids. The sequences in the SwissProt database were then searched to determine which of the candidate sequences shared the histone-specific patterns. See pages 59-60 and Tables 1 and 2. The patterns all include "don't care" positions and positions where a particular amino acid is expected. See Table 2.

On return of this application, the examiner should consider whether the disclosure of Rigoutsos anticipates or would have made obvious any of the pending claims, especially the claims that are not subject to any outstanding rejections as a result of this appeal. If the examiner determines that any pending claims are unpatentable because of Rigoutsos, an appropriate rejection should be entered.

Summary

We reverse the rejection based on 35 U.S.C. § 101. We affirm the rejections under 35 U.S.C. §§ 102(b) and 103 with respect to claims 1-3, 5, 8, 10, and 12 and reverse them with respect to claims 6, 7, and 11. We reverse the rejection under 35 U.S.C. § 103 with respect to claim 9 and the rejection under 35 U.S.C. § 112, second paragraph, with respect to claim 7. We affirm the rejection under 35 U.S.C. § 112,

[11] Rigoutsos et al., "Combinatorial pattern discovery in biological sequences: the TEIRESIAS algorithm," Bioinformatics, Vol. 14, pp. 55-67 (1998). Rigoutsos was cited on the Information Disclosure Statement filed May 27, 2003.

second paragraph, with respect to claim 4 but designate that affirmance a new ground of rejection.

Time Period for Response

Regarding the affirmed rejection(s), 37 CFR § 41.52(a)(1) provides "[a]ppellant may file a single request for rehearing within two months from the date of the original decision of the Board."

In addition to affirming the examiner's rejection(s) of one or more claims, this decision contains a new ground of rejection pursuant to 37 CFR § 41.50(b) (effective September 13, 2004, 69 Fed. Reg. 49960 (August 12, 2004), 1286 Off. Gaz. Pat. Office 21 (September 7, 2004)). 37 CFR § 41.50(b) provides "[a] new ground of rejection pursuant to this paragraph shall not be considered final for judicial review."

37 CFR § 41.50(b) also provides that the appellant, WITHIN TWO MONTHS FROM THE DATE OF THE DECISION, must exercise one of the following two options with respect to the new ground of rejection to avoid termination of the appeal as to the rejected claims:

> (1) *Reopen prosecution.* Submit an appropriate amendment of the claims so rejected or new evidence relating to the claims so rejected, or both, and have the matter reconsidered by the examiner, in which event the proceeding will be remanded to the examiner. . . .
>
> (2) *Request rehearing.* Request that the proceeding be reheard under § 41.52 by the Board upon the same record. . . .

Should the appellant elect to prosecute further before the examiner pursuant to 37 CFR § 41.50(b)(1), in order to preserve the right to seek review under 35 U.S.C. §§ 141 or 145 with respect to the affirmed rejection, the effective date of the affirmance is deferred until conclusion of the prosecution before the examiner unless, as a mere

incident to the limited prosecution, the affirmed rejection is overcome.

If the appellant elects prosecution before the examiner and this does not result in allowance of the application, abandonment or a second appeal, this case should be returned to the Board of Patent Appeals and Interferences for final action on the affirmed rejection, including any timely request for rehearing thereof.

AFFIRMED-IN-PART, REVERSED-IN-PART, 37 CFR § 41.50(b)

Demetra J. Mills)
Administrative Patent Judge)
)
)
Eric Grimes) BOARD OF PATENT
Administrative Patent Judge) APPEALS AND
)
Lora M. Green) INTERFERENCES
Administrative Patent Judge)

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